Vascular Diseases

Vaculitis: it's a pathological term characterized by inflammation of blood vessel wall lead to thickening of BV wall, thrombus in the lumen, perivascular inflammatory infiltrate and extravasation RBC.

etiology

1) Primary: →Idiopathic 50%

2) Secondary:

→infection: Bacterial GABH strept. Virus URTI – HCV.

→ C T disease : SLE, RA.

→ IBD (Inflamatoy bowel disease (ulcerative colitis , Crohn's)

→ Drugs → penicillin, sulfonamides,NSAIDs,Oral contraceptive

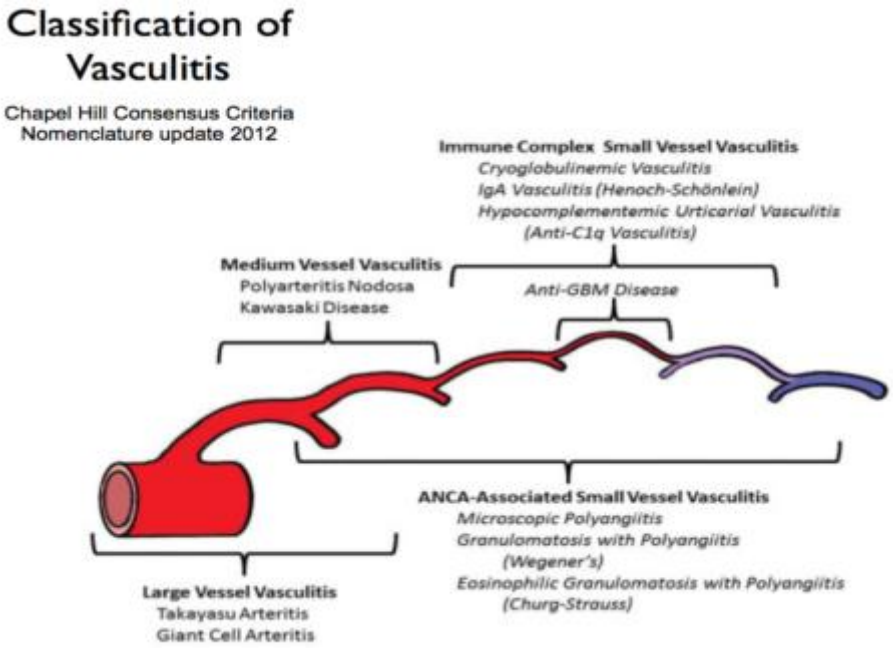
→Neoplasm→Haematological(Myeloproliferative–lympho proliferative)

Classification of Vaculitis

According to atiology
- **1ry**
- **2ry**

Accorging to size
- **small size BV**
- **medium size BV**
- **large size BV**

According to type of infiltrate
- **neutrophilic (leucocytoclastic)**
- **histiocytic (granulomatous)**
- **lymphocytic**
- **eosinophilic**



Pathogenesis

Immune complex mediated **ANCA – mediated**

(I) Immune complex – mediated vacuities.

* Type III hypersensitivity reaction.

Circulating antigen(infection,drug,chemical)→ bind to circulating antibody→Ag.Ab immune complex → deposition on blood vessels wall→activation of complement system → complement fragments C3a , C5a →lead to:

(1) increase adhesion molecule expression between inflammatory cell (Nenhroplis) and endothelium [E-selectin,ICAM1, VCAM1 , P- selectin]

(2) chemotaxis of Inflammatory cells: C5a → Neutrophils
C3a → Mast cell

(3) Degranulation of inflammatory cells →

(a) Neutrophils → Release of infl. Mediators + free oxygen radicals + proleolytic enzymes (collagenase + elastase) → vessel wall necrosis + thrombosis + occulosion + Haemorrhage.

(b) Mast cell→ Release & histamine + heparin→ increase VD + increasse permeability →extravasation of RBCs + Perivascular inflammatory infiltrate .

(2) ANCA mediated

Anti- Neutrophil cytoplasmic Antibody

* the Ag is intra cellular (Neutrophil) proteins :

(1) PR3 (proteinase 3) (2) MPO myeloperoxidase

*These Antigens expressed on Neutrophil cell surface→ formation of Anti body

C-ANCA → for PR3 & P-ANCA → for MPO

*ANCA → recognize the Ag → cellular activation → Release of Reactive oxygen species and toxic mediators→ vessel wall damage + chemotactic to Neutrophils → More inflammation.

Cutaneous small vessel vasculitis (CSVV)

Leucocytoclastic vasculitis,necrotizing vasculitis,hypersenetivity vasculitis

Cutaneous small vessel vasculitis (CSVV) are group of disorders characterized clinically by palpable purpra an histologically by leucocytoclastic vasculitis of postcapillary venules& fibrinoid necrosis.

Etiology:

*1- **idiopathic***

*2- **infection**: **bacterial (**GABH strept & staph aureus & M.leprae**)***
viral (hepatitis A,B,C & herps virus & influenza v***)***
fungal (candida albicans***)***
protozoa (plasmodium malariae***)***
helminthic (schistosoma & onchocerca ***)***

3- ***drugs :*** insulin & penicillin &tamoxifen & oral contraceptives vitamins & thiazides

4- ***chronic diseases :*** SLE & RA & behcet disease & ulcerative colitis &AIDs

*5- **malignancy:*** Hodgkin's disease & mycosis fungoides.

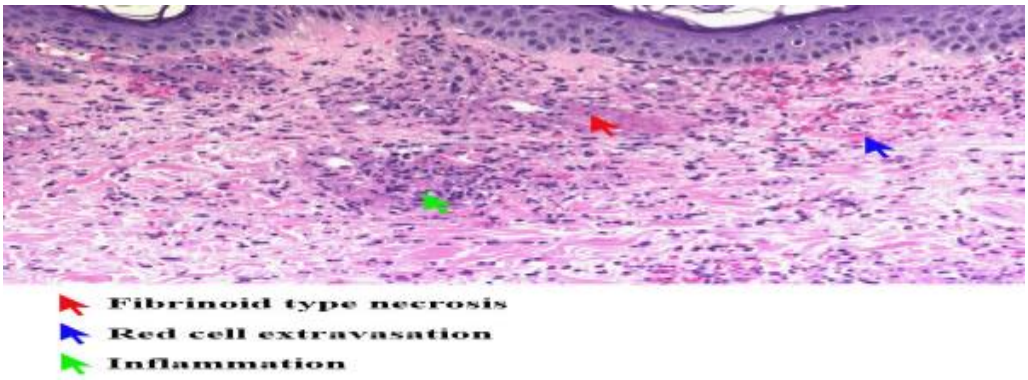
Clinical features:

- **Palpable purpra is the hallmark**. It may become papulonodular, vesicular ,bullous,pustular or ulcerated.
- it occurs mainly on legs and ankles.Uncommon sites are face , palms,soles and mucous membranes.
- It may be purpric or painful. On healing it leaves hyperpigmented or atrophic scar.
- Fever ,malaise and arthralgia may occur.
- **Systemic manifestations:**

Kidneys (nephritis , haematuria,protienuria , acute , ch. Renal failure)
GIT (colicy pain, NVD, melena, haematemsis)
Lung (cough , haemoptysis) **Heart** (pericarditis)
CNS (headache, diplopia, hypothesia,parathesia)
Joint (arthralgia , arthritis)
eye (retinal vasculitis,conjunctivitis, keratitis)

pathogenesis : **Immune complex – mediated vacuities.see before.**

Histopathology:



Leukocytoclastic vacuities

- Angiocentric segmental inflammation
- Endothelial cell swelling
- Fibrinoid necrosis of BV wall, post capillary venules.
- Cellular infiltrate within and around BV wall composed of neutrophils with fragmented nuclei (Karyorrhexis or leucocytoclastic).
- Extravasation of RBC ►Thrombosis of post capillary verules.

DIF: deposition of (IgG,IgM,IgA and complement C1q , C3 and fibrin) within post-capillary venular wall.

Treatment;

1st line:

- R/ of causative agent.
- Supportive care
- Symptomatic releife ; NSAIDs, Antihistamines.

2nd line:

- Colchicine (0.6 mg bid-tid)
- Dapson (50-200 mg/day)
- Systemic steroids (60-80 mg/ day)
- Hydroxychloroquine

3rd line:

- Azathioprine(2mglkg/day) 100-200 mg/day
- Methotrexate (<25mg / week)
- IVIgs.
- Plasmapheresis.

((Urticarial Vascuitis))

Pathogenesis:

* type III hypersensitivity reaction :

Circulating immune complex →deposition on BV wall →complement activation lead to:

(1) activation of mast cell Release of infl. Mediator TNF ∝ lead to:

1. increase ICAM expression on mast cell eosinophilia trans migration
2. E-selection on endothelial cell

(2) activation of complement pathway C3a , C4a, C5a→ Chemoattraction of neutrophils →Release &proleolytic enzyme →Vascular inflammation

Diagnosis : clinically – histopathologic – Lab investigation

(1) Clinically: pain ful, persistant urticaria which is not blanch on pressure and heal with Hyperpigmentation

The disease Spectrum

Hypo complementic cases

Major criteria
Urticarial > 6 months
Hypo complemetemia

Minor criteria
- cutaneous vaculitis on biopsy
- Abdominal pain
- arthralgia
- glumerulonephritis
- Low C1q level.

Normo complementic co cases
Disease is skin limited

(2)Lab investigations: ↑ESR , Hypocomplementemia,↓ circulating immune complex

(3)Histopathology: Leukocytoclastic vacuities

- Angiocentric segmental inflammation
- Endothelial cell swelling
- Fibrinoid necrosis of BV wall, post capillary venules.
- Cellular infiltrate within and around BV wall composed of neutrophils with fragmented nuclei (Karyorrhexis or leucocytoclastic).
- Extravasation of RBC
- Thrombosis of post capillary verules

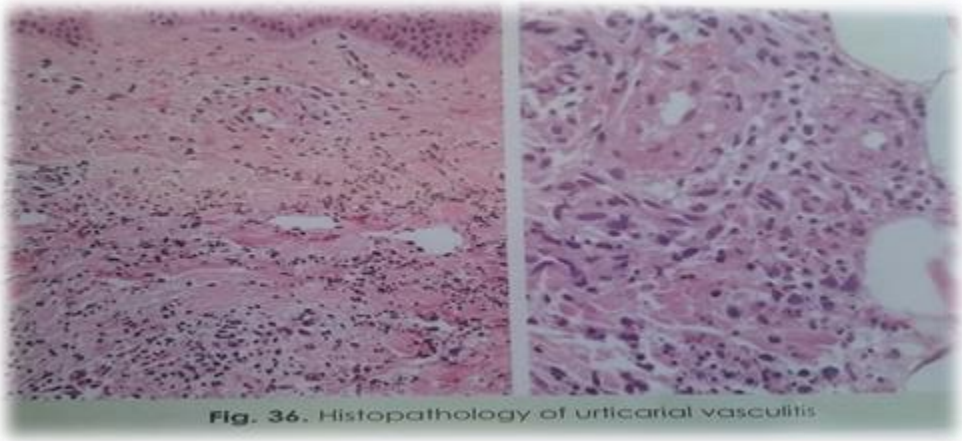


Fig. 36. Histopathology of urticarial vasculitis

Treatment

1st line

- H_1, H_2 blockers→Antihistamine (Allergex)
- 3rd generation Anti histamine (Fexofenadine)
- NSAID: Indocid – Brufen
- Corticosteroid
- Dapson (100-200 rg) + pentoxifylline

3rd line

- Mycophenolate mofetil
- IVIg
- Cyclosporine
- plasmapheresis
- Rituximab

2nd line

- Colchicine 6 mg 1x2
- Hydroxychloroquine (200 – 400 mg/ day)
- Azathioprine or Methotrexate

((Henoch-Schonelin Purpara))

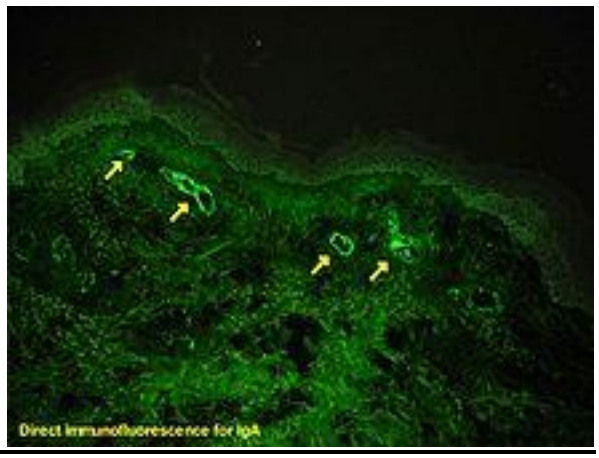
(Anaphlactoid purpura)

The most common Vaculitis in children mainly boys (2-11 years) usually following Respiratory tract infection (GABH strept).

C/P **PAPAH**

- **P**alpable purpura (all cases): symmetrical, hemorrhgic
- **A**bdominal **p**ain (61-67 %) of colicy pain, vomiting, melena, Hematemesis
- **A**rthralgia and Arthritis common in Knee, ankle
- Renal changes: Acute focal or diffuse GN → **H**ematuria

Death is due to renal failure.



Direct IF: IgA, C3, Fibrinogen within blood vessel wall .

American college of Rheumatology criteria of HSP:

2 or more yield specificity 87.7% , sensitivity 87.1% :

1- Palpable pupura

2- Age ≤ 20 year at onset of Disease

3- Bowel angina → Diffuse Abd pain ↑after meal , bloody diarrhea

4- Vessel biopsy →qranulocytes in wall of arterioles or venules.

Treatment

1st line

supportive care (bedrest)
NSAID for arthralgia

3rd line

Mycophenolate mofetil
Rituximab
IVIg
Plasma pheresis

2nd line

* systemic Corticosteroid For treating arthritis , abdomen pain
But not prevent recurrence or renal disease
* Dapson , colchicine →↓duration of skin lesion
* Azathioprine ± syst CST.

((ANCA associated vasculitis))

Anti _Neutrphilic cytoplasmic Anti bodies Attacking intracellular proteins (PR3, MPO) of the neutrophils.

the main 3 ANCA associated vasculitis:

1) Microscopic polyangitis 2) Wegener's granulomatosis

3) churg-strauss syndrome (Allergic granulamatosis).

Churg-strauss syndrome	**Wegener's granalomatosis**
Necrotizing granulomatous vascuitis +Asthama + Eosinphilia.	Triad of 1) Granulomatous inflammation of upper & lower respiratoy tract 2) systemic necrotizing small vessel vascuitis . 3) pauci-immune qlomerulonephritis
Pathogenesis: * tissue infiltration then degranulation of eosinophils → tissue injury * T-helper 2 help in granuloma formation * ANCA dependent activation of neutrophils.	ANCA binding to PR3 → vessel damage (pauci_ immune Or non – immune complex mediated vasculitis)
Clinical features: 3 phases **1st phase** → Allergic rhinitis, nasalpolyp asthma. **2nd phase**→ peripheral eosinophilia respiratory tract infection, GIT symptoms. **3rd phase**→ Systemic vasculitis with granulomatous inflammation. **Cutaneous findings** : palpable purpa followed by s.c nodule in scalp + extremities.	Urticarial, maculo-papular erythematous lesion. PG is uncommon in early stage. * Peri-auriclular lesion destroying the ear may be the earliest manifestation. * death is due to renal failure **ROUGH** **R**adiograph → abnormal chest **O**ral ulcer **U**rinary sedementation is abnormal **G**ranulomatous inflammation on biopsy **H**emoptysis.
Lab: eosinophilia ANCA against MPO --> 60% ANCA against PR3 --> 10-15% **Histopathology**: * eosinophilic infiltrate *extravascular granulomas * Necrotizing vasculitis in small, medium size BV	Leucoctlosis + Anaemia C-ANCA against PR3 → 80% of cases ↑CRP ↑ ESR
R: 1st line →systemic CST 2nd→ cyclophosphamide 3rd→IVIg, Mtx, Azathioprine , plasmapheresis Rituximab, mycophenolate mofetil	Systemic CST prednisolone (1mg/kg/day) + oral daily cyclophosphamide * IVIg, Mtx, Azathioprine , plasmapheresis Rituximab, mycophenolate mofetil

((Cryoglobulinemia))

- Cryoglobulins are abnormal immunoglobulin that precipitate at low temp (below body temp < 37) and redissolved by heating, cryoglobulins may deposited as immune complexs in small vessels lead to cryoglobulinemic vasculitis.

- 3 types type (1) single monoclonal IgM common >Ig G > IgA
Type (2) Mixed monoclonal IgM>IgG
Type (3) Mixed polyclonal IgM + IgG

Aetiology:

- **Idiopathic.**
- **Secondary**
  - **infection (syphilis , leprosy , HBV , HCV, HIV)**
  - **Autoimmune (SLE , SJS , RA)**
  - **Neoplastic (Myeloma , Lymphoma).**

Clinical Picture:

Figure 2: Severe Digital Ischemia Leading to Necrosis in a Patient With HCV-Related Mixed Cryoglobulinemia—HCV = hepatitis C virus.

- **palpable purpura.**
- erythematous macules, Nodules, ecchymosis, infarction, hemorrhagic crust and ulcers over legs.
- Systemic → Arthralgia 70% in small, large joint
  → Fatigue, liver, Renal, pulmonary involvement
  → Peripheral neuropathy&lymphadenopathy& splenomegaly.

Histopathology: → small vessel Neutrophilic vasculitis

DIF: granular deposition of IgM + C3

- PAS stain : eosinophilic PAS + ve globular immune complex deposits

Tests: Cryocrit estimation of the packed volume of precipitate after centrifugation of Pre-cooled serum ± gel elechopheresis.
- ↑ESR - ↑ Ig Level - +ve Rheumatoid Factor - skin biopsy
Treatment: 1) R/ of underlying disease(interferon+ ribavirin in HCV)
2) NSAID for arthralgia 3) Avoid cold
4) CST 5) Azathioprine
6) Anti-malarial 7) plasmapheresis 8) Rituximab.

Erythema Nodosum

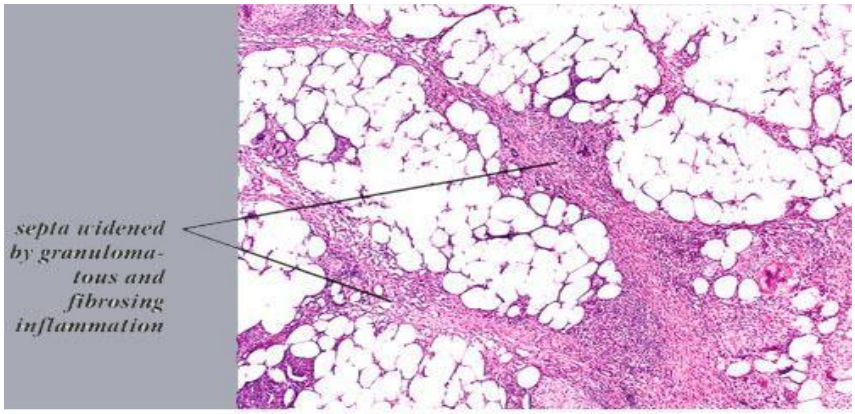
- The most common type of panniculitis (septal panniculitis without vasculitis)
- Characterized by erythematous nodules typically found in peritibial areas. It's acute inflammatory / Immunologic reaction disorder of s.c tissue.

Causes:

- **idiopathic** 30%
- **Infection**: Bact: GABH strept, TB, salmonellosis,
  Viral → infect. Mononucleosis, HBV
  chlamydia → LV, cat scratch.
  Mycosis→kerion, blastomycosis ,histoplasmosis.
- **Drugs**: oral contraceptives, sulphonamide.
- **Malignancy**: Leukemia, Hodgkin's

Female: male 3:1
Pathogenesis: reactive erythema due to many causes it may be due to immune complex that deposited in and around deep dermal BV and adipose tissue But??**DIF** couldn't demonstrate any Immuroglobulins in BV wall.
C/P

Red nodules: Bilateral, symmetrical, tender in the peritibial areas. The lesion associated with fever , arthralgia,leucocytosis . the progress is acute and regress with bruise like color that remain for months with no ulceration.



Histopathology: septal panniculitis without vasculitis

- Septal inflammatory infiltrate + septal vascular endothelical swelling + edema, haemorrhage.
- The infiltrate extend to fat lobule by lace – like fashion
- There is lymphocytes, histiocyte, Giant cell, No leucocytoclastic vasculitis or fat necrosis.
- Miescher's microgranulomas (diagnostic) (characthistic) they are present is the septa. Consisting of small, well defined nodular aggregation of small histiocytes around a central stellate or banana shaped cleft.

Lab : ↑ESR, ↑ASOT, Leucocytosis, Anemia

x-ray chest Abnormal (hilar adenopathy or infiltrate)

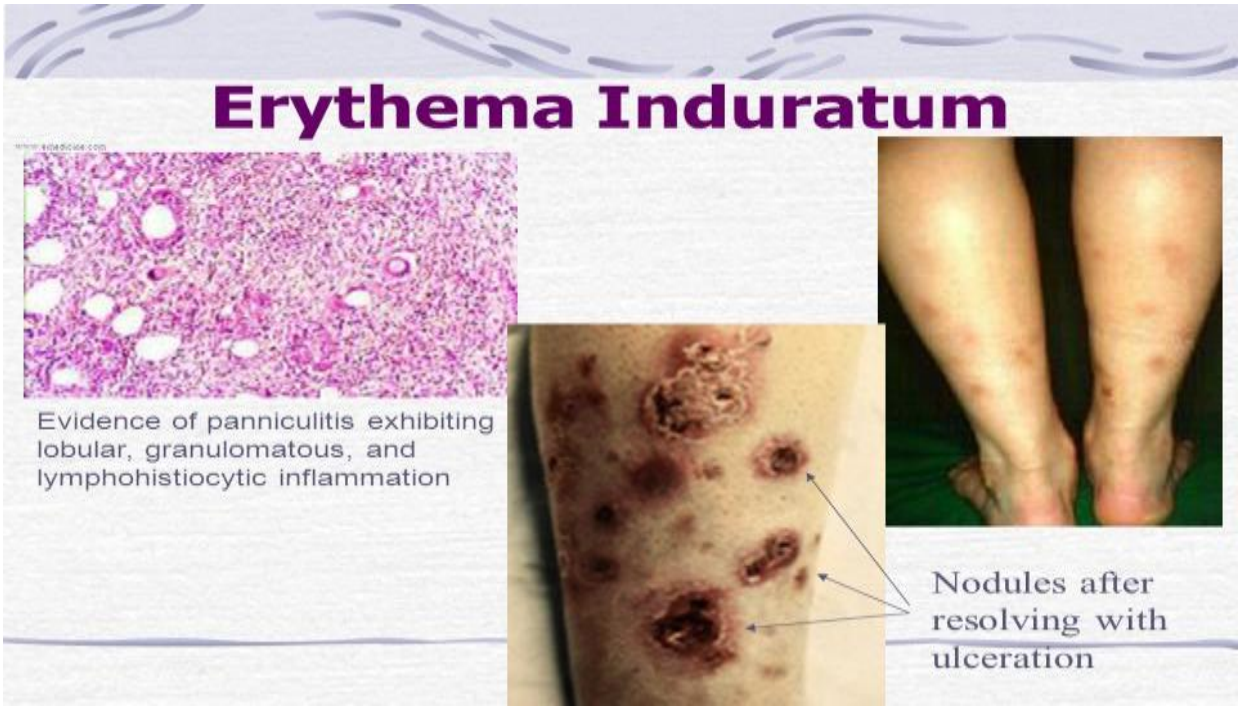
D.D:

1) Erythema indurate of basin → more in claves, ulcer, scar formation.
2) Erythema N.Leprosum: in L. Leprosy, with leucoytoclastic vasculitis
3) polyarthritis Nodosa: small pruritic nodules , ulcerate, leucoytoclastic vasculitis

Treatment: 1) R/ of underlying cause 2) Bed Rest
3) NSAID: Acetyl salicylic acid, Indomethacin
4) K+ iodide 900 mg/ day or as solution(2-10 drops on orange juice 3 times daily for 3-4 weeks it lead to heparin release from mast cell→ inhibition of DHR, inhibit neutrophil chemotaxis.

Nodular Vasculitis

Erythema induratum of bazin(tuberculous cause)
Erythema induratum of whitfield(Non – tuberculous cause)
It's a form of Lobular panniculitis with S.C vasculitis.



C/P :

Erythematous nodule, tender or asymptomatic, S.C found in posterior aspect of Leg. ulcreation and oozing occur. They remain for long time healing with scar. they may be associated with ischemic changes (cool, edematous skin) Venous insuficiency and varicose veins occurs.

Pathogenesis: Immune complex vasculitis triggered by different Antigens. Mycobacterial DNA has been identified by PCR in **Erythema induratum of bazin**.

Histopathology: Lobular panniculitis with mixed Infiltrate .

Medium size vasculitis is often present → ischemic necrosis of Fat lobule →granulomatous inflammation consist of(Lymphocytes, histiocyte, giant call, epitheloid cell).

Caseous necrosis is present in 50% & Cases ever if the Cause is Not TB.

Treatment

1- Antituberculous drugs for cases associated with TB
2- Bed rest
3- Tetracyclines
4- NSAID
5- Potassium iodide
6- Dapson
7- systemic steroid.

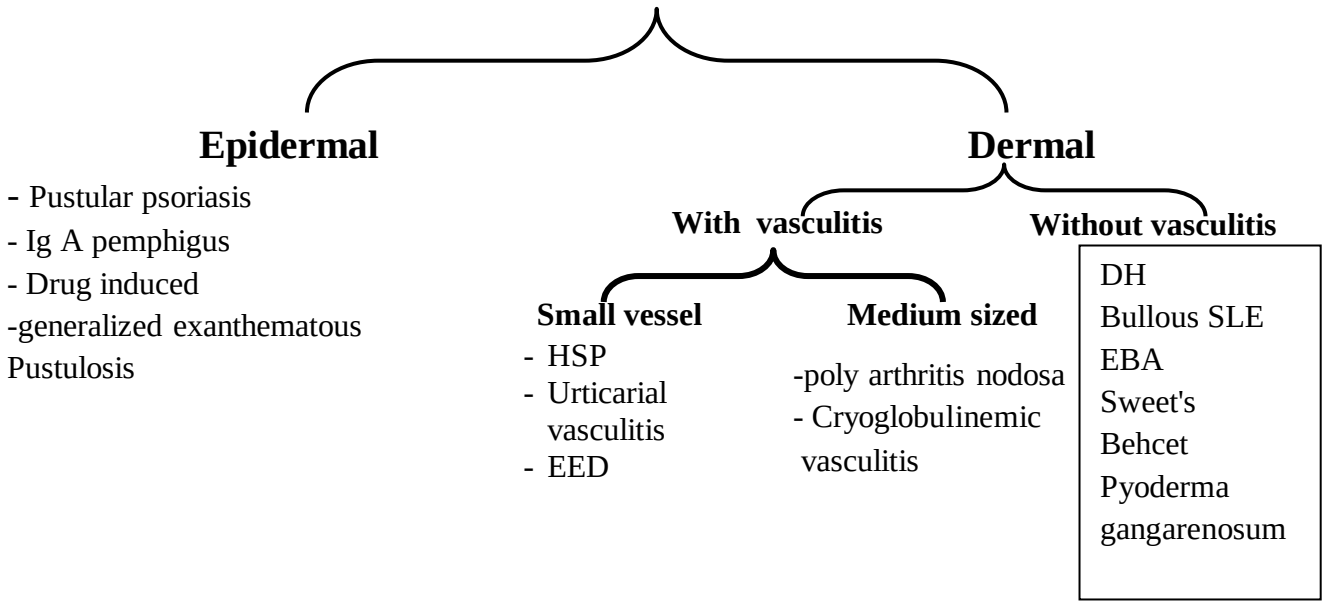
Neutrophilic dermatosis

They are group of diseases Characterized histologically by Neutrophilic infiltrate without infectious agent (sterile pustules)

the (4) Classic Neutrophilic dermatosis are :

1- Sweet's syndorne
2- Pyoderma gangarenosum
3- Erythema elevatum Dintiunm EED
4- Behcet disease

There are many types & non infectousdermatosis:



Pyodema Gangrenosum

Non infectious neuhophilic dermatosis associated with systemic disease.

***Aetiopathogenesis*→Unknown but it may be:**

a) Immunologic abnormality associated with systemic diease.

b) Defect in cell mediated immunity &Humoral immunity.

Clinical variets:

1- Classic ulcerative: commonest, painful lesion, fever, malaise arthralgia. the lesion is papule or plaque→ ulcerate with violaceoue undermined border, erythematous purulent base. the ulcer extend rapidly and heals by cribriform scar.

2- Pustular PG: multiple steril pustules surrounding a halo of erythema.

3- Bullous PG: heamorrhagic bullae associated with hematological disease

4- Superfacial vegetative PG: Usually follow trauma or surgery & often solitary vegetative or ulcerative lesion.

Associations:

1- Inflammatory bowel disease & ulcerative colitis & Crohn'sdisease .

2- Arthrits.

3- Blood diseases: Leukemia

Diagnostic criteria

Major	Minor
1- Rapid progression, painful, necrolytic ulcer, with violaceous border, undermined edges , erythematous base	1- Presence of associated systemic disease
2- Exclusion & other causes & skin ulcer	2- Clinical finding of cribriform scar 3- Rapid response to corticosteroids 4-Histopathology (Not specific) - steril dermal Neutrophilia ± Mixed in flammation ±Lymphocytic vasculitis

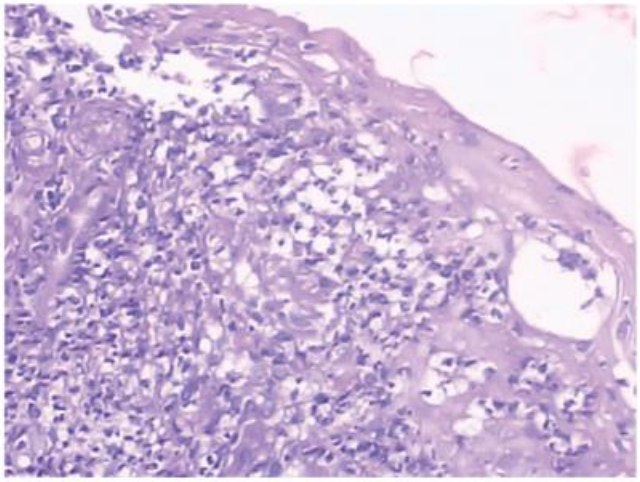


Figure 3. *Superficial diffuse dermatitis with an inflammatory process at base, and deep dermatitis with the prevalence of neutrophils, compatible with PG - hematoxylin-eosin (H&E) 5x.*

Diagnosis by one Major and 2 minor at least

Treatment → Aim →
- Control the underlying disease
- ↓Inflammatory process,
- Induce healing

1) General measures (ulcer Care)

Compression – limb elevation – skin grafting -Flap repairs -Dressing

2) Mild cases:

- Intra lesional CST
- Superpotent topical CST
- Oral Artibiotics
- Dapson(50 – 150rg)twice daily

3) Sever Cases:

Prednisolone 60 – 120 mg daily

Cyclospoine 2.5 – 5mg / kg / day

Iv Ig 2-3 gm/kg IV slowly.

4) Treatment of associated Disease.

Sweet Syndrome

Acute Febrile neutrophilic Dermatosis

Epidemiology: Age → Any age Female > male (4:1)

Etiopathogenesis: unknown but may be :

- **(1) Genetic:** Abnormality of chromosome 3q, ↑ incidence with **HLA-B54**
- **(2) Hypersenstivity Reaction**:

♦ Ig and Complement–mediated activation and mobilizalion of neutrophilis.

♦Antigen or superantigen – induced T-cell dependent cellular immuine Reaction.

- **(3) Immune Cytokine dysregulaltion** (local or systemic) Certain Cytokines and chemokines may help in initiation and propagation of inflammatory process of sweet syndrome.eg: IL1 , IFN γ , GM_CSF , G_CSF

GM_CSF :Granulocyte–macrophage colony stimulating Factor.

G_CSF : Granulocyte colony stimulating Factor.

Clinical Features:

- **FHMA**
- **Cutuaneous manifestations**: Acute onset of asymmetrically distributed Bright red –to purple, painful tender, warm, sharply demarcated plaques which have mamillated surface. the lesion may be annular, arcute, acneiform.**Site:** Face , trunk , upper extremities**.**
- Oral and genital lesion are rare but may be occur.
- **+ve pathergy test:** development of specific skin lesion at the site of minor truama or injury(by needle) it's positive in 8% only.
- Resolve spontaneously within 5-12 weeks but may recurrent in 30%.


- **Extra cutaneous manifestations:**
    - Serum sickness symptoms: Myalgia, Malaise, headache, N .

- Musculoskeletal →arthralgia , arthritis of elbow,knee
- Ocular→ iritis,conjunctivities, iridocyclilis.
- Respiratay→ cough, dyspnea, pleurisy, P.effusion.
- Renal →Haematuria, proteinuria, Acute Renal Failure.
- Meningeal→ Meningitis (Aseptic), encephalilis.
- GIT →hepatitis ,pancreatitis, GIT upsets.

Diagnostic Criteria:

1- Major: skin lesion + histopathological finidings

2- Minor: 1- Preceded by fever or infection

2-Fever > 38°c

3-leucocytosis

4- Associated with extracutaneous manifestations.

5- Dramatic Response to systemic steroid or potassium Iodide

No response to systemic Antibiotics

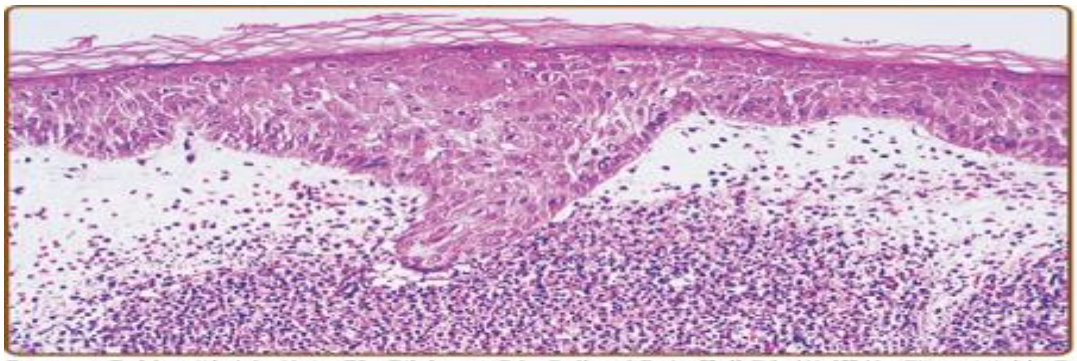
How to diagnose→ 2 major + 2 minor

Histopathology:

1- Upper and mid – dermal perivascular diffuse Neutrophlic infiltrate

2- Papillay dermal edema.

3- Leukocytoclasia (**nuclear dust**) with endothelial swelling, vasodilatation, extravasation of erythrocyte but without fibrinoid necrosis DD of vasculitis



Source: Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, Wolff K: *Fitzpatrick's Dermatology in General Medicine, 8th Edition*: www.accessmedicine.com

massive edema of the papillary dermis and a dense diffuse infiltrate of mature neutrophils throughout the upper dermis (hematoxylin and eosin stain)

Lab findings:

- ↑ESR
- Leycocytosis
- Neutrophilia
- ↑CRP
- Antineutrophile cytoplasmicAntibodies(ANCA)

Association with sweets syndrome

1- Malignancy:

Leukemias – Breast cancer – Ovarian cancer-Endometrial Cancer, Vaginal cancer, Rectal Caner, Prostatic , testicular Cancer.

2- Inflammation:

ulcerative colitis, Crohn's disease, Cirrhosis,subacute thyroiditis ,Behcet syndrome, Rheumatoid arthritis , Pyoderma gangrenosum.

3- Infection:

S: Staph, strept ,salmonella.

H:Hepatitis , HIV, histoplasmosis

Meningitis , TB

4- Others: Drugs, pregnancy , Renal stone , Immunization, photo_induction

Treatment

- Anti biotics is ineffective until if associated with Bact infection.
- Topical R/ in few or localised lesion
  topical CST OR Calcineurin inhibitors.
- Systemic R/
  - Prednisolene (0.5 – 1.0)mg/ kg / day for 4-6 weeks.
- Dapsone(100 – 200mg/day)
- Cyclosporine (5-10mg/day) ↓ production IL1.
- Indomethacin 50 mg
- Potassium iodide 900mg /day
- Colchicine

Behcet disease

*** Chronic multisystem disease characterized by:**

Oral, qenital aphthae + cutaneous lesions + ocular manifestations, arthritis + GIT manifestations + Neurological manifestations.

D.D with other aphthosis(constant more than 3 oral or genital with No systemic manifestations)

Pathergy test: injection of 0.1ml saline by 20-22 gauge sterile needle at 5mm depth or **+ve result** show papules or pustules with in (24-48hours).

Pathogenesis:

Genetic: Associate é HLA – B51

Infechion: HSV, HCV ,Parvorirus, strept strains

Autoimmune response:

♦Pt with behcet has higher circulating immune complexes.

♦Role of Neutrophils in chemotaxis→ More neutrophils →activation , release of Ros , Lysozomal enzyme → Tissue damage

♦Role of Cytokines IL 12 →activate Th1

IL 8 → Neutrophil chemoattractant

Clinical manifestation:

1) *Mucocutaneous*:

- ***Recurrent aphthus stomatitis***: painful, 1-3cm, shallow or deep é yellowish fibrinous base, herpitiform ulcer pin point lesions arranged in clusters. Healing with No scar.

- ***Recurrent qenital ulcer*** → they tend to heal with Scar

- ***Skin lesion***: papules, pustules, acneiform eruptions.

tender nodules on leg EN- like. The skin reactivity increase by scratching and pathergy test. Self limited healing steril pustules.

2*) Systemic manifestations*:

- **Ocular:** can be painful → blindness.
  - Retinal vasculitis – Ant, post uveitis, 2ry glucoma, cataract
  - Inflammation (conjunctivitis , scleritis, vitreous Hge, optic neuritis).

-**Neurologic:** Acute meningo – encephalitis cranial Nerve palsies.
- **Joint:** athritis , Mono athritis – Poly athritis (knee , wriste , ankle).
- **GIT:**Abd. Pain, ulceration ,haemorrhage.
- **Renal:** GN
Vascular: Aneurysm or thrombosis.

Histopathology:

Vasculopathy affecting all sizes of blood vessels.
Neuhophilic vasaular reaction – leucocytoclastic vasculitis
With or without thrombosis or necrosis.

Treatment

Mucocutaneous disease
- Viscous lidocaine topical sucralfate
- Topical or Intralesional CST
- Dapson
- Colchicine
- Dapson + Colchicine

Sever Mucocutaneous disease
- thalidomide (50-150) at night
- Methotrexate (2.5-5mg) weeky
- Prednisolone (40-80 mg) day
- infliximab (TNF α inhibior)
- interferon α-2a.

Systemic disease
- prednisolone (60-120 mg) day
- Azathioprine
- Mycophenolate mofetil
- IVIg
- tacrolimus

Common Causes & oral ulcers:

Local causes $\rightarrow$ oral SCC
Ulcers associated with systemic diseases:
Blood: Anamia , leukemia

GIT → Coeliac disease ,ulcerative colitis , crohn's disease.

Rheumatic→ LE, sweet's syndrome

Cutaneouse disease: Pemphigus – Erosive LP – EM – DH

Vasculitlis: PAN, wegener's granulomatosis

Microbial disease: Herpetic stomatits, chicken pox ,HZ, hand food mouth disease

Drug induced : Methotrexate – Mercury poisoning .

Livedo reticularis

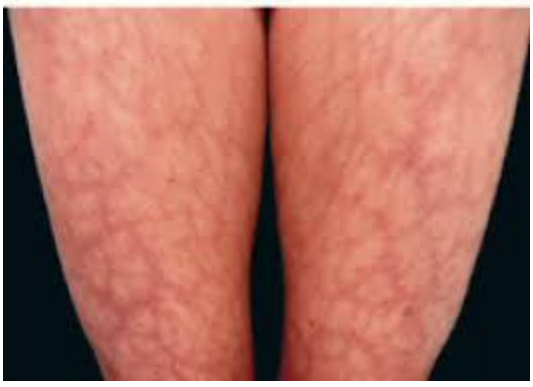
It is a cyanotic , mottled discoloration of the skin with a characteristic network pattern which is accentuated by cold . it's persistent and doesn't respond to rewarming.

Causes:

(1)Physiological
(2)Intravascular obstruction
→ emboli eg cholesterol
➔ Hypercoagulopathy
➔ Paraprotienemia (cryoglobulinemia)
(3)Vessel wall disease
(4)Arteriosclerosis
(5)Metabolic : hyperparathyroidism, hypercalcemia
(6)Arteritis: vasculitis → polyarthritis nodosa.
(7)CT disease : LE, SLE,DM
(8)Idiopathic
(9)Congenital
(10) Miscellaneous : drugs,pancreatitis, capillary nevi.

Pathogenesis:

The blood supply of normal skin is arranged in cones , their bases 1-4 cm across on the surface of skin , each supplied by arteriole.
The mottling of livedo reticularis follows this pattern.
The color changes is due to dilatation of capillaries and stagnation within the capillaries and minute venules in the dark areas.

Clinical varietis : according to the nature of underlying cause.

(1) A complete fine network:

Indicates alternation of blood flow caused by vasospasm or by factors within the blood that alter the viscosity and the flow through the vesseles.

(2) Patchy distribution :

Indicates vessel wall pathology and intramural obstruction

(3) Livedo racemosa :

Consists of large branching pattern that is usually situated on the trunk and proximal limbs. It's indicative of sneddon's syndrome or antiphospholipid antibody syndrome

N.B***: sneddon's syndrome*** : Extensive livedo reticularis and cerebrovascular disease eg : hemiplegia and aphasia